

## **REMARKS**

In the current office action, the Examiner allowed the claims of Group I (claims 1-4) to be examined with the claims of Group II (claims 5-19 and 27-39). In making this determination, the Examiner stated that the claims of Group II included claims 5-19 and 27-29 (rather than 27-39 as stated on page 2 of the office action dated 10-05-2005). The Applicants assume this was a typographical error and have replied in the current office action on the basis that claims 5-19 and 27-39 are covered under Group II.

The Examiner rejected claims 1-19 and claims 27-39; claims 20-26 and 40-60 were withdrawn from consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention. The Applicants have requested claims 7, 10, 14, 18, 20-26, 33 and 40-60 be cancelled and claims 1, 3, 4, 6, 8, 13, 27, 31, 32 and 34 be amended. No new matter is introduced as a result of such amendment.

### **Objections to the Specification**

The Examiner objected to the specification for failure to comply with 37 CFR 1.821-1.825 regarding the disclosure of SEQ ID NO.: 16 in the specification. The Applicants have corrected SEQ ID NO.:16 in the specification and claims to agree with the computer readable form. The Applicants have also amended the specification to refer to a 24 residue sequence rather than a 25 residue sequence where appropriate.

The Examiner also objected to the specification for containing a hyperlink. Applicants have requested the specification be amended to delete reference to the hyperlink.

### **Rejections Under 35 USC 112**

The Examiner rejected claim 4 under 35 USC 112 second paragraph. The applicants have amended claim 4 to remove the term “about”.

The Examiner rejected claims 1, 2, 4, 6-19 and 27-29 under 35 USC first paragraph. The applicants have amended the claims 6, 13, and 27 such that the DNA repair modulator recites a single chain antibody having the sequence of SEQ ID NO.: 17 or that includes the CDRs of SEQ ID NOS.:18-23; claims 7-19 and 28-29 are dependent on and incorporate the limitations of one of claims 6, 13, or 27. The applicants have also made the same amendment to claim 32.

With regard to claim 1 and the claims dependent thereon (and also claim 37 and the claims dependent thereon), the Examiner states that the claim is inclusive of a genus of DNA repair modulators and that the specification does not provide sufficient descriptive information such as definitive structural or functional features that are common to the genus of DNA repair modulators. The Applicants respectfully disagree with the Examiner's statements regarding the written description with regard to claims 1-4.

The specification clearly teaches that the beneficial effects on inhibition of DNA-PKcs are obtained by virtue of binding a DNA repair modulator to a region outside the catalytic site of the DNA-PKcs, specifically, to a site on the DNA-PKcs having the sequence of SEQ ID NO.: 16. This finding was a unique contribution. The prior art was not aware of the utility of SEQ ID NO.: 16 prior to the Applicants' work. Furthermore, claim 1 (and claim 37) requires that the DNA modulators (and single chain antibody) bind to a polypeptide region having the sequence of SEQ ID NO. 16. This limitation regarding binding to SEQ ID NO.:16 is a functional feature that is well described and supported by the specification and which is common to the genus of DNA repair modulators falling within the scope of claim 1 (and claim 37) and the claims dependent thereon. One of ordinary skill in the art would be able to use the teachings of the application to identify other compounds that bound SEQ ID NO.: 16. The current specification provides exemplary methods for carrying out such identification (see page 33, lines 4-22). Therefore, the Applicants respectfully submit that claims 1-4 (and 37-39) in their current form comply with the requirements of 35 USC Section 112 second paragraph.

### **Rejections Under 35 USC 102**

The Examiner rejected claims 1-19 under 35 USC 102(a) as being anticipated by Li et al (Nucleic Acids Research, 2003, 32(20):5848-5857). The Applicants have submitted an Affidavit under 37 CFR 1.131 stating that the applicants were the sole inventors of the material described in the aforementioned reference. As per the holding of In re Katz, 687 F.2d 450, 215 USPQ 14 (CCPA 1982), such declaration is sufficient to remove the Li et al. publication as a reference under 35 USC 102(a) (See also MPEP 715.01(c)).

The Examiner rejected claims 1-4, 6, 8, 9, 11-13, 15-17 and 19 under 35 USC 102(b) as anticipated by Carter et al (Mol. And Cell. Biol., 1990, 10(12):6460-6471). The applicants have amended claims 6 and 13 such that the claims recite a single chain antibody not disclosed by Carter et al; claims 8, 9, 11-12, 15-17 and 19 are dependent on and incorporate the limitations of one of claims 6 or 13.

With regard to claim 1, the Carter reference does not teach or suggest the possibility that the monoclonal antibody disclosed binds a polypeptide having the sequence of SEQ ID NO.: 16. In fact, the Carter publication did not definitively identify the enzyme to which the monoclonal antibody bound as being DNA-PK. On page 1469, Carter et al. state “DNA-PK appears to be a novel type of protein kinase. If the 300 kDa polypeptide is indeed the enzyme...” Later on the same page, Carter et al. state “We cannot at present rule out the possibility that DNA-PK is another protein that strongly associates with the 300kDa polypeptide and requires this association for its stability in vitro but is present in such small amounts that it is not easily detected by silver staining.” Furthermore, Carter et al did not appreciate the fact that their DNA-PK enzyme was composed of two subunits- the regulatory Ku protein and the catalytic subunit DNA-PKcs. While the monoclonal antibody taught by Carter et al. inherently bound a sequence of DNA-PK, the inherency did not teach or suggest the sequence bound by the antibody. As disclosed in the Li et al. paper, significant investigation was required to determine the sequence bound. Therefore, Carter et al. could not have taught or suggested that the monoclonal antibody described bound to the sequence specified in SEQ ID NO.: 16.

### **Rejections Under 35 USC 103**

The Examiner rejected claims 1-19, and 27-29 under 35 USC 103(a) as being unpatentable over Li et al., in view of Kelley et al. (US Patent No. 6,252,048) and Jang et al. (Molecular Breeding, 2002, 9:81-91).

The Applicants have submitted an Affidavit under 37 CFR 1.131 stating that the applicants are the sole inventors of the material described in the Li et al. publication. The Kelley and Jang references teach the use of a nuclear localization signal to a DNA repair modulator and a chloroplast localization signal to a polynucleotide construct, respectively. The teachings of

Kelley and Jang do not teach or suggest a DNA repair modulator comprising a single chain antibody.

The Examiner rejected claims 1-19 and 27-29. The Examiner rejected claims 1-19, and 27-29 under 35 USC 103(a) as being unpatentable over Carter et al, in view of Bejcek et al (Cancer Research, 1995, 55:2346-2351), Kelley et al. and Jang et al.

The Examiner stated that it would have been obvious of one of ordinary skill in the art to take the monoclonal antibody as taught by Carter et al. and create the single chain antibody as taught by the present application given the teaching of Bejcek. Bejcek disclosed methods for the production of single chain antibodies from monoclonal antibodies and further disclosed the advantages of producing such single chain antibodies. Specifically, the Bejcek reference teaches the production of three single chain antibodies to the CD19 antigen.

However, the Bejcek paper explicitly states having possession of a monoclonal antibody does not translate into having a single chain antibody that binds the same target as the monoclonal antibody. In the introduction, Bejcek states that "One problem with the production of antibody binding domains in this manner is that high affinity antibody binding cannot be successfully reconstituted in all instances. The parameters that govern the ability of an antibody to yield an scFv that can bind its target are unknown, thus necessitating the direct cloning and analysis of the candidate antibody gene segments" (see page 2346, second paragraph). Furthermore, in the discussion section, Bejcek states that "Because the effects of primary amino acid sequence on protein folding are not well understood, there is no known a priori method for determining the ability of a particular antibody to function when produced in an scFv." Indeed, the results of the Bejcek paper bear this out. The single chain antibody designated FVS193 did not appear to bind to its CD19 target. Therefore, until a single chain antibody was produced and tested for the functional effects claims in the current application, one of ordinary skill in the art could not have known that such an antibody could be produced. The Bejcek reference is simply an invitation to experiment in order to create a desired single chain antibody.

Therefore, the Carter paper in combination with the Bejcek paper does not disclose or suggest a method for producing a single chain antibody that : (i) is a "DNA repair modulator

that specifically binds to the sequence KKYIEIRKEAREAANGDSDGPSYM (SEQ. ID NO.:16), or a portion thereof, and inhibits non-homologous end joining" as disclosed in claim 1; (ii) or where "the modulator inhibits DNA repair by specifically interacting with DNA-PKcs outside of the DNA-PKcs catalytic domain" as claimed in claim 6; (iii) or where "the modulator interacts with a DNA repair polypeptide and sterically inhibits the DNA repair polypeptide" as claimed in claim 13; (iv) or a "single chain antibody inhibits DNA repair by binding to a DNA repair polypeptide" as claimed in claim 27.

The Kelley and Jang references are discussed above and do not provide the teachings of the Carter and Bejcek papers.

### **Conclusion**

For all the reasons given above, the Applicants respectfully submit that the amendment to the claims define and distinguish over the prior art currently of record. Applicants respectfully request the application be processed for allowance.

Respectfully Submitted,



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